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WHAT ARE PELLAGRA AND PELLAGROUS INSAN-
ITY? DOES SUCH A DISEASE EXIST IN SOUTH
CAROLINA, AND WHAT ARE ITS CAUSES?

AN INQUIRY AND A PRELIMINARY REPORT TO THE SOUTH
CAROLINA STATE BOARD OF HEALTH.

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STATE HOSPITAL FOR THE INSANE,
COLUMBIA, S. C., Dec. 30, 1907.

GENTLEMEN:

The medical members of the board of regents and the medical staff of the State Hospital for the Insane beg respectfully to submit to your attention the following report:

Introduction.—By way of introduction we wish to say that, like other physicians of our acquaintance, we have from time to time been perplexed by the appearance of a disease presenting the mental symptoms of depression or mild delirium combined with an eczematous condition of the exposed surfaces of the body, especially of the hands and face, and usually the third symptom of an obstinate diarrhoea. Several of our cases have shown at home in different parts of the State mental symptoms of such pronounced character as to require commitment to an asylum. Three outside cases have been seen in consultation.

The syndrome of skin, intestinal, and mental symptoms point towards a disease known in southern Europe as pellagra, but that disease has so rarely been suspected or recognized in this country that we find that other physicians, like ourselves, in studying their cases, have excluded pellagra because most authorities deny its existence in North America. This inquiry based largely upon clinical evidence and a study of the few original papers on the subject by Americans brings into question the truth of the last sweeping statement. We are satisfied that we are dealing with conditions very similar to those presented by true pellagra as described by authors, but of the real nature of the disease, especially as to its etiology we are in doubt—hence this inquiry.

The recent admission to our State Hospital for the Insane of three cases which present clinically the classical symptoms of pellagra has forced us to study them with especial care and to review the histories of cases previously observed besides looking up such literature as is available. We have also conferred with several experienced general practitioners in Columbia and Charleston and from them have secured assistance and advice as well as the histories of outside cases included as part of this report.

It is the opinion of the older members of the staff that cases presenting pellagrous symptoms have appeared among our patients for some years and that the real nature of the malady has not been fully recognized and determined, but that latterly it is becoming much more frequent among our patients. These patients have come from various parts of the State, being possibly somewhat more numerous from the Piedmont section.

Whatever its nature the disease is not infectious or communicable.

One of the objects of this paper, besides calling the attention of your board to what seems a distinct pathologic entity, is to ask your co-operation in directing the attention of general practitioners to its symptoms and occurrence, and thereby gain a fuller knowledge of its distribution, causation, and prevalence than is possible for isolated observers like ourselves.

PART I. GENERAL. WHAT ARE PELLAGRA AND PELLAGROUS INSANITY?

Definition and Description.—What then is pellagra? Van Harlingen (1) calls it "A complex disease characterized by three classes of symptoms:

1. A squamous erythema confined to those portions of the skin which are exposed to the action of heat and light.
2. A chronic inflammatory condition of the digestive passages shown chiefly by obstinate diarrhoea.
3. A more or less severe lesion of the nervous system, leading at times to mental alienation and paralysis. These various symptoms are at first insignificant, and in a certain way periodic—they begin or recur in spring, and diminish or disappear in winter. Later, they become persistent, more and more marked, and finally terminate fatally."

Griesinger (2) in 1861, after seeing cases of pellagra in the asylums of northern Italy doubted the specific nature of the disease, but thought that in its final state it greatly resembled general paralysis of the insane.

In 1883 Spitzka (3), of New York, announced in his excellent treatise on insanity:

"Pellagrous insanity will not be discussed in this volume, as it does not occur in America, and is limited to such countries as Italy, where maize forms a staple article of diet and where the disease known as *pellagra*, which is attributed to the living on spoiled maize, occurs in an endemic form."

Says Manson (4) in 1907: "Indeed there are vast regions in which maize is extensively cultivated and much eaten, but in which pellagra is absolutely unknown. A most convincing example is that of the United States of America."

Says Tyson (5) in Ziemsen's Cyclopedia:

"Pellagra is a disease which is thought to be due to a fungus which infects maize or Indian corn. It occurs particularly in Lombardy, and is characterized by a scaly and wrinkled condition of the skin, especially of those parts exposed to the air. The strength and mental faculties are affected. Sensation is obtunded and cramps and convulsions supervene, much as in ergotism."

Macpherson (6) in 1899 expressed the opinion that:

"Pellagra is a disease of the nervous system accompanied by mental symptoms and followed often by degeneracy in the descendants. This transmitted degeneracy is characterized by mental and physical feebleness and a marked predisposition to the recurrence of the affection in the predisposed offspring. The disease is common in the southern parts of Europe, especially in Italy, and has been indubitably traced to the eating of immature and otherwise unwholesome maize."

From Mendel (7), of Berlin, we learn that:

Pellagra "shows in the prodromal stage general distress, fatigue easily brought on, disturbances of digestion, usually with areas of redness of the skin, which is chapped, cracked, and deprived of epithelium. The second stage is dominated by pathological phenomena of the intestinal tract, and the third stage shows, besides disturbances of the nervous system (weakness and

pareses, paresthesias and anthesias, weakening of the cutaneous reflexes and exaggeration of the tendon reflexes) a melancholic depression, which often passes to the stuporous form."

It will thus be seen that true pellagra appears to be akin on the one hand to ergotism and lathyrism and on the other to the paretic forms of insanity, while in some of its manifestations it is not unlike acute delirium.

History.—The earliest account of this malady as an endemic affection comes from Spain, where it was recognized in 1735. It appeared in Italy just prior to 1750, and was first scientifically investigated in 1771. It first appeared in southwest France in 1829. Its present distribution embraces the districts of Europe situated within a zone extending from 42° to 46° N. It is found also in Egypt and Asia Minor. Sandwith found it in 1900 among the colored lunatics on Robben Island (4).

The disease attacks males and females indiscriminately, and no age is exempt. Cases are on record of children of 14 months and 2½ years of age. Under sanitary and preventive management it is claimed that pellagra has almost disappeared from France, but there are in Italy 100,000 cases of the disease, that is, 10 per cent of the rural population. About 10 per cent of pelligrous cases become insane. It is said that there are upwards of 50,000 cases of pellagra in Roumania.

There is a voluminous literature on the subject in Italian, French and German, as is shown by over eight pages of bibliography in Vol. XII, Second series, of the Index Catalogue of the library of the surgeon general's office in Washington. But in English, outside of short accounts or definitions of the disease in the text-books, articles are few and far between.

Although recognized now as existing in Yucatan and Campeche, as well as in Brazil and the Argentine Republic, pellagra has rarely been reported as being found in the United States.

In April, 1907, however, Dr. G. H. Searcy (8) read before the Alabama State Medical Association an account of an epidemic of acute pellagra in the State Hospital for Colored Insane at Mt. Vernon, Alabama. Since the opening of the hospital in 1901 three or four cases of a strange and fatal skin disease had occurred, but its true classification was not recognized. In the late summer and early fall of 1906 the epidemic appeared. In all 88 cases occurred

with 57 deaths, a mortality of about 64 per cent. Since the observation of these cases among the colored insane patients some four or five others have been recognized among the white patients at the Tuscaloosa (Ala.) asylum.

In the report for 1907 of the Alabama insane hospitals by Dr. J. T. Searcy, superintendent, just received, it is stated that: "there was last fall (at the Mt. Vernon Hospital) an epidemic of pellagra, which was very fatal. This being a heretofore unknown disease in America, it was not recognized as such for some time. Cases have, since then, been brought into both hospitals from different parts of the State, showing that it occurs in this part of the country. There have been nine deaths at the Bryce Hospital during the past 12 months from pellagra, five of them were infected when they came."

A sporadic case diagnosed as pellagra was reported by T. C. Merrill, M. D. (9), of Colorado, Texas, in September, 1907.

Symptoms.—Usually the disease first manifests itself in the spring, the earlier symptoms pointing to the gastro-intestinal tract and the cutaneous structures, while the later and more advanced symptoms involve the cerebral and cerebro-spinal systems.

In his monograph (1903) Procopiu (10) gives this definition:

"Pellagra is a periodical disease, having remissions and exacerbations. It manifests itself in persons exposed to its invasion at the beginning of spring, becomes more aggravated until summer and then begins to lessen little by little to the point of giving during the winter the illusion of cure. It returns each year at the same season, so long as the cause persists, that is, the eating of the products of Indian corn."

Says Radcliffe-Crocker (11) in substance:

At first there is weakness and lassitude, giddiness, headache, articular pain, severe pain in back radiating to the limbs, especially the hands and feet; the tongue is furred, the epigastrium tense and painful, and the bowels are loose, sometimes with slight jaundice. The skin of the forearms, elbows, face, and neck are affected with dermatitis. The erythema may develop in 24 hours and last 10 to 18 days. It consists of a diffuse, dark or livid red erythema, which disappears on pressure unless hæmorrhagic. The skin is swollen, tense, and itches when exposed to the sun. After two weeks the erythema subsides; desquamation follows, leaving

the skin thickened and pigmented. The nails and hair are unaffected. After several attacks the skin dries, withers and wrinkles. The skin manifestations thus present three stages: (1) Congestion; (2) thickening and pigmentation; (3) atrophic thinning.

Upon recrudescence after the first attack the patient becomes emaciated and weak, with headache and pain in back and tenderness on pressure near the dorsal vertebræ, the knee jerk is exaggerated. The tongue gets denuded, is red and dry; there is a burning sensation in the mouth, deglutition is painful, diarrhœa increases to profuseness; all the cerebro-spinal symptoms, many of them meningeal, are aggravated, and the patient is delirious, sinks into a typhoid state and dies.

Mental Symptoms.—These usually assume the type of melancholia. The milder forms show merely a retardation of ideas, disinclination for thought and activity or simple mental depression. Later the disease may advance to a profound melancholia, even refusal of food, and suicidal tendencies manifesting themselves. Maniacal symptoms are rarer, but sudden outbursts of delirium or excitement may occur in cases of apparent stupor.

Clerici (12) (1855) described pellagrous insanity as consisting of "a vague, incoherent delirium, accompanied by stupor, loss of memory, and by loquacity without special disorder of intelligence or violent excitement."

Pellagrous insanity is divided by Procopiu (13) into acute and chronic delirium. The acute delirium may be associated with alcoholism, when it presents the symptoms of delirium tremens. Or acute delirium may manifest itself in the course of chronic delirium. In the latter case the patient who has been quiet and apathetic, becomes restive as if tormented by an obsession. The delirium may become furious, leading to suicide or murder. Intense religiousness may be a symptom or food may be refused. The chronic delirium has been divided into the melancholy, demented and stuporous types, but pellagrous patients usually suffer from melancholia of an anxious type. The termination is dementia.

"Pellagrous insanity," says Régis (14), "is one of the most grave varieties, not in itself, but because it is the expression, in the sphere of intelligence, of a general disease, progressive in its course, and inevitably ending in cachexia and death."

Says Warnock (15): "The frequent early occurrence in pellagra of symptoms of dementia, with loss of memory and childishness points to organic brain disease, and reminds one of the mental condition of patients suffering from organic dementia due to gross brain lesions, and of the later stages of general paralysis. Indeed, the last stage of a general paralytic of the melancholic type and that of a pellagrous patient have many resemblances to one another."

Etiology.—Among the abandoned theories about the origin of pellagra may be cited those of its being an expression of leprosy, scurvy, syphilis, or alcoholism.

Tuczek (16) concludes that "pellagra is due to certain toxic substances developed in the course of the decomposition of Indian corn and, possibly, under the influence of epiphytes on the corn." "The maize cut before it is ripe, gathered in rainy seasons, stored away damp, sown from affected seed, . . . all contribute to the engendering of some toxic development in the grain which forms the true pellagrous poison."

From the dermatologist's (17) side it may be cited:

"Pellagra is believed to be due to the consumption for long periods of time of damaged maize, this being the staple article of food in most of the countries where the disease is endemic. The eating of the grain harvested before it is fully ripened, particularly in regions where famine has existed, the harvests are poor, and the lower class of the rural population live in insalubrious conditions—is the chief factor in the production of the malady.

"Persons of both sexes and all ages are liable to contract the disease; heredity is supposed to exert an influence, especially when the nervous symptoms of the malady are predominant. The sporadic cases occurring where there has been no suspicion of the ingestion of improperly prepared food are believed to represent a 'pseudo-pellagra' having a wholly different etiological history."

A sample of the meal used at the Mt. Vernon (Alabama) Hospital (18), which was supposed to be the best western meal, was sent to the pathologist in charge of the Laboratory of Plant Pathology at Washington, and he reported that "the meal was wholly unfit for human use; that it was made of mouldy grain and con-

tained quantities of bacteria and fungi of various sorts, some of which were identified."

Dr. Merrill (19) also referred some of the corn meal that had formed his patient's diet to the Laboratory of Plant Pathology at Washington. The pathologist reported that the meal was unfit for regular diet, being "unquestionably in bad condition and too rancid to eat, at least for a regular diet."

Radcliffe-Crocker (20) sums up the etiology alliteratively: peasant life, poverty, and polenta (a food made from maize).

"Pellagrous insanity," says Bianchi (21), is a "disease arising from intoxication of the nervous system," and further that "Ceni and Besta concluded that both *Penicillium glaucum* and *Aspergillus fumigatus* play very important part in the etiology of pellagra, and that their action can be explained only by their determining phenomena of progressive intoxication by means of the toxins they set free in the gastro-intestinal canal."

But after all that has been said and written upon the etiology of pellagra, there seems yet to be doubt as to the ultimate cause, as witness this extract from Novy (22) in Osler's Modern Medicine (1907):

"While there is no question as to the fact that the poisoning is due to corn, the actual cause, notwithstanding the numerous investigations which have been made, is by no means established. It is reasonable to believe that the specific toxic products are formed by the action of some bacterium on the maize which has been cut while immature and stored in damp condition."

Diagnosis.—In cases (23) where the nervous symptoms are especially prominent, the diagnosis has to be made from neurasthenia and hysteria. Here we must consider etiology.

While the history, periodicity in the spring, and increased knee-jerk will help distinguish between the affections, the exanthem may be absent, but when present without symptoms it must be distinguished from pure solar erythema. The condition of the tongue and intestinal tract will assist in the diagnosis. If the spinal symptoms primarily attract attention, the coincident mental disorder, the erythematous eruption, and the gastro-intestinal lesions will determine between pellagra and a pure neurosis.

Other diseases to be excluded are: Ergotism, lathyrism, beriberi, scurvy, eczema, lichen, uncinariasis (hook-worm disease)

acute delirium, alcoholism, syphilis, and paresis. In brief *pellagra* may be said to present a triad of symptoms: Dermatitis, diarrhœa, and depression. The more prominent skin symptoms are erythema, dessication, and desquamation; those of the digestive system: salivation, dyspepsia, and diarrhœa; and of the nervous symptoms: headache, backache, spasms, paralysis of legs and melancholia. In our colored patients the dermatitis, diarrhœa, and consequent emaciation, as well as the dementia and paresis, have been strikingly well marked. The disease is said sometimes to exist without the eruption—a condition called “*pellagra sine pellagra*.”

Pseudo-pellagra.—Occurs in chronic alcoholism with peripheral neuritis, and is said sometimes to appear in asylums among the demented and general paralytics. In the latter case it is more likely a pseudo-general paralysis, since true paresis does not present the skin or intestinal lesions of pellagra. “The disease is pellagra when it fits in with the orthodox theory and when it can be connected in any way with maize, but when this is not possible, the disease becomes ‘a pseudo-pellagra.’” (Manson (24).)

Ergotism.—History of diet (usually rye), headache, vertigo, mild delirium, blindness, deafness, anæsthesia, cramps, convulsions, and gangrene.

Lathyrism.—History of diet (vetch); pains in the kidneys and lower extremities, spastic paralysis, possibly paraplegia, increased knee-jerk, ankle clonus. Intelligence clear.

Scurvy.—History of food conditions, earthy complexion or jaundice, depression both nervous and mental: pain in limbs and joints, indurations and ecchymoses, visceral hæmorrhages, stomatitis.

Beriberi (24).—Peripheral multiple neuritis, sometimes ascribed to a diet of rice, œdema, or emaciation, severe effusions, slight hydrothorax, general dropsy, ataxia, partial paralysis, great muscular weakness; knee-jerk lost or impaired, ankle-drop, palpitation, precordial distress; pericardial effusion, systolic bruits, violent carotid throb; anæsthesia in pretibial region and hyperesthesia in calf and other groups of muscles. General health good; may be dyspepsia, but tongue clean and bowels fairly regular. Urine may be scanty but otherwise normal. No fever. Intellect not involved. *Filaria*, *anchylostomum*, and other worms are very commonly

found in beriberi. Manson concludes that beriberi is a germ disease, but probably not communicable from man to man.

Lichen.—Roundish papules, small or large, chronic in course, and appears on anterior surfaces of arms above wrists, lower part of abdomen, calves of legs, and around knee. It may appear on palms of hands and soles of feet. Hair and nails unaffected. General nutrition never affected in *L. planus*. Prognosis favorable with tendency to spontaneous recovery.

Eczema.—The common symptoms of infiltration and thickening of the skin with exudation and itching which characterize this disease are not associated with the conditions of the gastro-intestinal and central nervous systems which make up the clinical picture of pellagra.

Acute Delirium.—Fever, delirium, great motor excitement, and rapid exhaustion, ending frequently in coma and death. Duration from 10 days to 3 weeks. No cutaneous or intestinal lesions.

Hook-worm.*—More or less pronounced anæmia followed by rapid exhaustion. Tallow-like skin in which you seem to see through the upper into the lower layer. There is an absence of perspiration which is frequently complete. The skin and hair are dry. The heart is found to be enlarged, with the apex beat displaced. Hæmic murmurs are common, as are also cervical pulsations. There is usually considerable abdominal tenderness shown by even slight pressure on the epigastric region. This tenderness has the decided tendency to continue, on palpation towards the right, but disappears toward the left side.

About 60 per cent of the cases show scars on the skin with the history of sores of long standing. About 85 to 95 per cent give history of "ground itch." In cases in which the anæmia began before puberty there may be total absence of hair in axillary and suprapubic regions. In affected females the menses are retarded and irregular, and rarely accelerated.

The symptom of "pot-belly" is common, though not as common as usually supposed. The pupils are usually dilated, even when facing a strong light. If not dilated, they dilate very readily when looking into the observer's eye, and sometimes even when

* Diagnostic symptoms as dictated by Dr. Ch. Wardell Stiles, of the U. S. Public Health and Marine-Hospital Service.

facing a strong electric light. The most pronounced mental symptom as a diagnostic aid is a low grade of mentality, or rather of dullness or stupidity, as indicated by repeating a question or asking that it be repeated. This is exceedingly common. This dullness, however, is cleared up in a striking manner after the exhibition of thymol. The tendency is to constipation rather than to diarrhœa, though some cases have diarrhœa. The seasonal periodicity shows an acceleration in summer and fall. The disease is much more common among people in sandy regions than in clay regions. Usually if one case occurs in a family, several others are found infected.

Pellagra, or at least pellagrous symptoms, may be associated with some of the above mentioned diseases as well as with malaria, tuberculosis, traumatism, and the eruptive fevers such as typhoid or diphtheria. Here the diagnosis is to be made only after careful exclusion.

The diagnostic symptoms of the other more common diseases mentioned need not be introduced here.

Prognosis.—The disease may run an acutely fatal course or an extremely slow one. (Searcy.) Our experience has been that after admission to the asylum the duration of cases will scarcely average six months. Cases having severe diarrhœa, emaciation, and delirium run a rapidly fatal course in spite of the usual treatment. In Europe, it is said, pellagra may run through 10 or 15 years. Recovery can be expected only when the patient has passed through one or two annual spring attacks, is removed from the cause, and is placed in hygienic surroundings. If the disease is far advanced, the prognosis is unfavorable, as it is also when permanent nervous lesions appear, such as chronic insanity, or motor paresis.

PATHOLOGY.

General.—Wasting of adipose and muscular tissues, fragilitas ossium, degeneration of the cardiac muscular tissue, fatty degeneration and atrophy with slight degree of sclerosis of the liver, spleen, and kidneys.

Constant.—(a) Intestinal: atrophy, of muscular coat, with occasional hyperemia and ulceration of lower part of tract.

(b) Abnormal pigmentation (like senility) of ganglionic cells muscles of the heart, the hepatic cells, and the spleen.

(c) Changes of nervous system. By far the most important and constant post mortem signs: Hyperemia, anemia, œdema of central nervous system, pachymeningitis, cerebral and spinal leptomeningitis, obliteration of spinal canal.

Most noteworthy and constant: Degeneration and secondary proliferation of the lateral columns of spinal cord in dorsal region but also of posterior columns in cervical and dorsal regions.

Treatment.—The questions of prophylaxis and treatment, although of highest importance do not properly come within the scope of this inquiry, but may be summed up in the fundamental principle of discovering and removing the cause.

In Europe the usual method is to prohibit corn in any shape and form as food, or, if this is impossible, permit the use of only such grain as is ripe to perfection, is well dried, and stored, and which is the result of sowing of good quality. The cultivation and use of other cereals is to be encouraged.

The nervous symptoms of the disease are treated according to general therapeutic indications. There is no specific. If hook-worms are found associated with pellagra they should be removed by thymol.

Before taking up the consideration of our cases this paragraph taken from Warnock's (26) paper on "Pellagrous Insanity" will prove interesting:

"Pellagra is never uncomplicated in the stage seen here (the Cairo, Egypt, Asylum). Every patient suffers from parasitic diseases. Favus, often producing complete baldness, is frequently present. The anchylostomum worms are always present, and the resulting extreme anæmia accounts partly for the great prostration of these cases. Other intestinal worms often occur. Bilharziosis of the rectum or bladder affects many cases and further aids the development of the anæmia and exhaustion. In fact, it is a matter for astonishment that an individual preyed on by so many kinds of parasites is able to survive so long. Many of these patients have a dried-up wizened look, suggesting that of a mummy."

Furthermore, as to the likelihood of erroneous conclusions by reason of the secondary or accidental association with hook-worms this quotation from Manson's (27) "Tropical Diseases" in regard to beriberi is pertinent:

"The novice in tropical medicine will be greatly puzzled for a

time over these cases. . . . If he examine the blood of these patients, possibly in a proportion of them, he will find filaria nocturna or some other blood worms; very likely he will then think that the cases are forms of filariasis, and he may construct theories to explain how the filaria produces the symptoms. Or if he examines the feces, very probably in over 50 per cent of the cases, or in some countries in nearly all the cases, he will find the ova of anchylostomum duodenale, and, probably those of trichocephalus dispar also. On this evidence he may conclude that these are cases of anchylostomiasis. He had better, however, not commit himself to such a diagnosis, until he has ascertained how it fares with the rest of the population as regards these parasites, for he will find that the filaria, the anchylostomum, and the trichocephalus are quite as prevalent outside as inside the hospital, and in the healthy as well as in the sick."

In 1902 Dr. Harris, of Georgia, reported a case of anchylostomiasis, presenting the symptoms of pellagra:

A farmer first seen March 8, 1902, unmarried, aged 29 years, native and resident of Georgia. The patient had been reared in unusual poverty, the bread constituting his principal diet from infancy being always of Indian corn produced at home. When first seen his health had been bad in spring and summer for 15 years, being manifested by malaise, loss of appetite, thirst, melancholia and weakness and anæsthesia of legs. Later skin over hands, arms, and dorsal surfaces of feet became inflamed, blistered, and covered with scabs. He was constipated. Examination disclosed decided cachexia. Anchylostomum worms were found and a large number expelled by thymol. Later examination showed their absence. Patient reported that he was at first improved but later that he was no better than before treatment.

Dr. Harris writes that having lost sight of this patient he can give no subsequent history.

PART II. LOCAL. DOES SUCH A DISEASE EXIST IN SOUTH CAROLINA AND WHAT ARE ITS CAUSES?

CASE I.—M. C., admitted to State Hospital December 9, 1907, white, female, American, housekeeper, age 30 years, married 11 years, 3 children, no miscarriages. In this State one year. Previously for three years in Cleveland County, N. C.

Previous History.—Family very poor, but patient was healthy up to five years ago when menses ceased. In spring three years ago rash appeared on back of hands like sunburn, which spread in spite of treatment. Got

better in cold weather, but never entirely healed. Family produced all the corn they used. None of family or neighbors have had "eczema," but family physician said he had had a similar case. Patient developed symptoms of mental depression about two years ago, which subsequently have been continuous. Bowels have been constipated with occasional diarrhœa, the latter having been constant and severe for three months before admission. (See Plate I.)

On Admission.—Extreme adynamia, stupid appearance, reluctance to exertion. Sat with bowed head and spoke in monosyllables and only when spoken to. Muscular system fairly preserved. Axillary and suprapubic hair present. Poor appetite but intense thirst. Temperature 97 degrees; pulse 80, regular and full. Respiration 20. Urine normal, as shown by repeated examinations. Blood examination showed a relative increase of lymphocytes and a moderate degree of anæmia.

Gastro-intestinal.—Abdomen flat. Exhausting diarrhœa, sometimes as many as twenty stools a day, light yellow to copper color. Hook-worms and eggs found by several observers.

Skin.—Slightly jaundiced; eczematous condition covered forehead, also alæ nasi, malar bones and chin, as well as dorsal surfaces of hands and feet; very scaly and rough on exterior surface of elbows and knees. No sores or scars. Most of these regions were chapped and fissured. Anæmic and puffy about eyes.

Mouth.—Foul breath; tongue deep red and clean, straight and not tremulous.

Lungs.—Normal. Heart, accentuated aortic second sound.

Nervous and Mental.—Tendon reflexes exaggerated; tabetic gait; stiffness of muscles; dull and melancholy; suspicious about food; occasionally mildly excited. Pupils react to accommodation and slightly to light.

Has slightly lost ground physically and mentally since admission. Has become more and more paretic, so that she had to be put to bed. Temperature varies from 96 degrees to 99 degrees. January 1, 1908, she was given thymol grains 15. Thymol repeated January 12. Has made an assault upon an old woman sleeping in room with her.

After studying this case Dr. Stiles's comment was: "If this is hook-worm disease, its symptoms are entirely different from those I am familiar with, and without microscopic examination I should place her in the doubtful class as regards uncinariasis."

CASE II.—R. P., admitted to State Hospital, December 2, 1907, colored, male, age 30 years. History meager. Mother is said to have died of old age. Mental symptoms developed slowly. History of apoplectiform seizures. At times was incoherent and profane. Mind ran much on religion. Diarrhœa for three months, and eruption appeared on hands three months before admission. (See Plate II.)

Physical Examination.—Patient very emaciated and anæmic. Deep reflexes somewhat exaggerated. Heart, at times soft, blowing systolic mur-

mur, normal in size and position. Lungs negative. Abdominal organs normal, except a slight enlargement of the spleen. Some slight tenderness upon palpation over abdomen. Cervical and inguinal glands somewhat enlarged.

Skin.—Of the forehead and face and especially over malar bones and the back of the hands presents an erythematous-squamous eruption, cracked and fissured.

Mental Symptoms.—Those of depression and apathy; a marked indisposition to exert himself.

Temperature.—Either normal or slightly subnormal. Pulse average, 76. Respirations, 20. Appetite poor. Sleep normal. Very persistent diarrhœa, not yielding at all to the usual modes of treatment. Tongue and buccal cavity red, but with no tendency to hæmorrhage.

Died from exhaustion December 22, 1907.

CASE III.—L. D., admitted to State Hospital October 1, 1907, colored woman.

Previous History.—Married 20 years. Eight children. No miscarriages. In poor health six years. Worried over death of two brothers. Eruption appeared on face and hands two months before admission. No diarrhœa then. Mind affected two weeks before admission. Ten in family, but none of them had skin trouble; but woman neighbor had similar trouble from which she died. Produce the corn they use, except a little grits. On admission extremely weak. Paretic symptoms, increased knee-jerks. Muscular wasting. Heart: Systolic murmur at base. Lungs negative. Skin: Forehead, nose, malar prominences, and chin covered with an eczematous eruption. Dorsal surfaces of hands and feet and of elbows and knees, much thickened, darkened, chapped, and fissured. Obstinate and exhausting diarrhœa. Died of exhaustion December 26, 1907. (See Plate III.)

The spinal cords of Cases II and III were examined by Dr. F. B. Mallory, Associate Professor of Pathology in the Harvard Medical School and reported as "negative."

CASE IV.—Mrs. D. R. C., white. Seen in consultation with Dr. J. J. Watson April, 1906. Age 46 years, married, no children. No specific history.

In good health until 18 months previously. Then she became sleepless and "nervous" contrary to her habit. Soon afterwards she noticed a general weakness and an erythema appeared on the backs of her hands, extending from the metacarpo-phalangeal articulation to three or four inches above the wrist. No eruption on face, forehead, neck, or feet. Examination showed heart, lungs, and other organs normal, and this conclusion was confirmed by careful and repeated examinations. Pulse persistently between 90 and 100. Temperature, a. m., 97; p. m., 98 to 99.2. Skin on dorsal surfaces of hands extending above wrists showed a pig-

mented harsh and scaly condition. Patellar reflex exaggerated. Tenderness over spinal column in mid-dorsal region. Right pupil dilated.

Nervous Symptoms.—Persistent dull vertical headache. Was neurastheric hypochondriacal and melancholy. No diarrhœa, bowels regular. Under best hygienic and medical treatment for eight weeks, she did not improve. Since then she has been lost sight of.

Dr. D. S. Pope, of Columbia, recalls these cases, the records of which have been lost:

“About 15 years ago I had under my care at the South Carolina Penitentiary a case presenting this history:

CASE V.—White man, 40 years old, developed a crimson rash on the forehead and dorsal aspects of the hands. It was thought he had erysipelas, but it yielded very slowly to the usual treatment. The next spring the eruption returned in the exposed surfaces and extended to the cheeks, but it became of a squamous nature. He at this time developed an obstinate diarrhœa and the mental symptoms of melancholia. All treatment including stimulation proved of no avail. He became gradually exhausted and died during the late spring.

CASE VI.—About the same time I saw in private practice a white woman about 50 years of age, who had a scaly eruption on cheeks, backs of hands and neck, and a severe intractable form of diarrhœa. She was restless and delirious, and for this reason I was called in by the family to decide whether she was properly a subject for commitment to the asylum. We got a nurse and kept her at home, but she died from an exhausting diarrhœa about two years from the time the eruption was first observed.”

The appended histories and observations are furnished us by L. K. Philpot, M. D., of Columbia, physician to the Epworth Orphanage, an institution located in the suburbs of Columbia, and having an average of 150 white inmates, who come from every portion of the State.

“I hand you herewith reports of some interesting cases of what clinically might be termed ‘eczema,’ but which also present symptoms of other pathological conditions:

CASE VII.—Lilian M., age 6 years. History was that of a healthy child, quiet, and of average intelligence.

Father died at 50 years of age, of unknown cause; otherwise no family history obtained.

Clinical History.—An eczema with reddish base appeared upon the dorsal aspects of feet, ankles, hands, wrists, forehead, cheeks, and neck. The portions of the body covered with clothing were not eczematous. This condition continued for several months, when she developed diarrhœa and

began to lose flesh and strength. Shortly afterwards she began to show nervous and mental symptoms not unlike those of spinal meningitis. While sitting up she would gradually go forward until her head reached the floor or she would fall from the chair. Varied treatment, including specific remedies, produced no effect. Finally, hook-worms being found in her stools, she was given thymol and made a complete recovery.

CASE VIII.—Avery J., aged 10 years. Father and mother living and healthy. This child was well developed, both physically and mentally. A red scaly eczema appeared on the dorsum of both feet and hands, the ankles, wrists, forehead, cheeks and neck. No skin lesion on parts protected by clothing. He developed a diarrhœa, lost strength and flesh until he became a living skeleton. His condition did not yield to any treatment, either local or general. At this time hook-worms were found in very large quantity, but he was too feeble to take the usual treatment. He developed mental symptoms of a stuporous type and died of exhaustion.

CASE IX.—Morris L., aged 9 years. A rather delicate child, with no history. She, too, developed a scaly red eczema of the feet, hands, forehead, cheeks, and neck. Lost strength and flesh. After some months she developed violent insanity, with symptoms of a spinal meningitis, and died.

“Until within a few days of the death of Cases VIII and IX I did not know how to find the hook-worms, nor did I suspect that this parasite was the cause of the condition of my patients. At this time I met Dr. Ch. Wardell Stiles, of the U. S. Public Health and Marine-Hospital Service, and had him examine all the children at the orphanage. In 25 showing signs of eczema the hook-worm was found. By the exhibition of thymol the children were relieved not only of hook-worms, but of eczema also. They have since been in good health.

“The clinical histories of the three cases above cited, presenting the combined symptoms of eczema (ground-itch), exhausting diarrhœa, and delirium, show, to my mind, what would have been the fate of the other 25 but for the timely eradication of the hook-worm.”

We have had accounts of similar cases from other physicians, but have not been able to obtain their histories in time for this paper. We have had besides other cases in the State Hospital which help to give us a clearer clinical picture of the disease, but the records of them are not complete enough to be included.

We are aware that the histories and notes on our cases are not

as full as we should like, but we feel justified in making a preliminary inquiry and incomplete report at this time in order that it may be presented to your board, so as to be included in your transactions for 1907.

We also recognize that we are standing upon debatable ground and that while the questions we are raising may be somewhat novel in America, yet the problem of the origin and existence of pellagra as a pathological entity is an old or even a trite question in certain European countries.

Finally, answering the queries at the heading of this paper we feel justified in concluding from the evidence presented:

1. That true pellagra is a disease long known in southern Europe, due to eating defective Indian corn and manifesting itself in the spring by intestinal, skin, and nervous symptoms.

2. That pellagrous insanity is a mental condition usually of the melancholy type, developing in patients already suffering from pellagra, as shown by the pre-existing skin and intestinal lesions.

3. That we are satisfied that a pellagroid disease occurs in South Carolina, but whether it is the true pellagra of Italy remains to be proven, as our observations, though suggestive, are as yet too few for a final opinion.

4. That while the conditions described do not harmonize entirely with the descriptions of Italian and French pellagra—especially as regards the season of the year—yet at least they very closely resemble Egyptian pellagra even to the association with the anchylostomum worm.

5. That the condition we are dealing with is not the form of pseudo-pellagra sometimes described since it does not stop at the erythematous stage, but presents the triad of symptoms—dermatitis, diarrhœa, and depression.

6. That a form of mental disease has come under our observation that in its clinical aspects is identical with pellagrous insanity.

7. That the discovery of the hook-worm in some of our cases is a most interesting association with the disease, but whether etiological or not demands further inquiry.

8. That the probable occurrence of such a disease in South Carolina having been established further clinical and pathological research is called for.

9. That the relationship between mental symptoms and hook-worm disease (uncinariasis or anchylostomiasis)* and kindred diseases, especially in the southern States, should also be a subject of further investigation (29).

In justice to ourselves we may be permitted to state that we had arrived at the diagnosis of probable pellagra for our cases before we learned of the contributions of Searcy and of Merrill published in the *Journal of the American Medical Association* of this year. That is, we had been working at the problem independently and did not know of the observation of probable pellagra in the United States until we had completed our own observations, arrived at the above conclusions and reported them orally to your president and secretary, and were arranging them in their present form when our attention was called to the recent papers above referred to and now quoted from in this paper. The paper of Dr. Harris, of Georgia, is of especial interest because of the association with hook-worms. The report of the Alabama hospitals came as our paper was going to press. To all of these we acknowledge our indebtedness as strengthening the position we have taken in concluding that pellagra has existed, unrecognized, for some time in our State.

Through the courtesy of Dr. E. N. Brush, superintendent, Shepard and Enoch Pratt Hospital, we have been enabled to look up the following additional references to supposed cases of pellagrous insanity in America as well as to obtain abstracts from the reviews in English of some articles and monographs appearing in Italian upon some of the phases of the pellagra problem.

In the *American Journal of Insanity* for October, 1864, Dr. John P. Gray of the State Lunatic Asylum, Utica, N. Y., reported a "Case of Pellagra of the Insane":

Male, age 31, enjoyed good health during childhood and adolescence and was mentally normal. Four years before admission he had an attack of

* As this article is going to press a paper on "Uncinariasis," by Dr. William Weston, of Columbia, appeared in the December number of *The Journal of the South Carolina Medical Association*, in which a case is described, showing such mental symptoms that lunacy commitment papers were being taken out, but hook-worms being found, commitment was delayed. On the removal of the hook-worms the mental symptoms completely disappeared.

"acute rheumatism" and since then has suffered from pain in back of head, shoulders, and back. Shortly afterwards suffered from weakness of arms and general lassitude. Subsequently symptoms of indigestion set in. Appetite was capricious and thirst was marked. Showed bad judgment in selling farm and became suspicious of his neighbors. Under delusions left home and wandered in woods for ten days. On return was emaciated and exhausted. Melancholia being recognized, he was committed to asylum, September 10, 1863. Soon after admission erythema appeared on hands and face. Examination disclosed scaly eruption over whole face, arms from elbows downwards, and legs from knees down. His bowels were at first costive, but with the appearance of the eruption diarrhœa set in. Later face deepened in hue and began to swell. He complained of intense pain in back of head, the skin became dark purple, parchment-like, and was cracked in places. Vesicles appeared, which exuded a yellowish white serum. The hands and feet continue to swell, deepen in color, crack and form vesicles, one crop succeeding another. He complained of intense itching and burning heat. All his joints appeared stiffened so that any motion gave intense pain.

He gradually improved under Fowler's solution and good nourishment.

The patient had never eaten maize to any extent. When constipated, the redness increased, but was relieved of both by an aperient.

In October, 1864, the physical and mental symptoms reappeared.

In the discussion, Dr. Tyler of the McLean Asylum, Somerville, Mass., said he had had for five or six years under observation a case which he had been unable to classify but which he recognized from Dr. Gray's description as pellagra. Dr. Pliny Earle said he had seen a similar vesicular disease at the Milan Insane Asylum 25 years before and reported them in Hays' Journal of 1840.

In reviewing this case (The Journal of Mental Science, April, 1866, p. 117) Arlidge was indisposed to regard it as a genuine instance of pellagra. Because "experience has shown oftentimes on an extensive scale the production of scaly and other eruptions on the skin in company with profound cachexia, and even mental disturbance as the result of improper food; but the maladies so engendered though etiologically allied to pellagra, could not be referred to as examples of that disease. For instance, Rayer has pointed out the relation between pellagra and the morbid consequences of eating spurred rye, and between that disease and the epidemic prevailing in Paris in 1828 and then described as acrodynia."

In the *Journal of Mental Science*, October, 1863, p. 353, Dr. James De Wolff, superintendent of the Hospital for the Insane,

Halifax, Nova Scotia, reports "A short Note on Some Cases of Pellagra," describing an epidemic in which 15 patients or about one-tenth of the household were affected with a disease presenting the symptoms of swelling and itching of both hands, of deep-blue color, fissures across the knuckles in a few instances. The color was too deep and persistent for erysipelas and too localized for purpura or scorbutus. Except for a certain degree of lassitude no constitutional symptoms presented themselves. No cause for the epidemic was discovered in diet or surroundings. Dr. De Wolff's paper was communicated by Dr. W. A. F. Browne, Commissioner in Lunacy for Scotland, who does not commit himself as to diagnosis but says that various observers have described a condition peculiar to the insane confined in asylums and regarded by them as a variety of pellagra, if not as the typical affection. It is characterized by emaciation, weakness, diarrhœa and in a more advanced stage by an erythema of different colors, but generally red or dusky, which follows exposure and covers the back of the hands, the arms, feet, neck, there being concomitantly an earthy or bronzed tinge of the skin, which is dry and rough. The eruptions may be vesicular, papular, squamous or furunculoid."

Lombroso's "Clinical and Experimental Studies on the Nature, Cause and Treatment of Pellagra" (Bologna, 1869) is reviewed in the *Journal of Mental Science*, January, 1872, p. 579, by J. R. Gasquet and these abstracts are made therefrom:

Dr. Lombroso proves pellagra to be a well-defined disease, produced by a special poison and that the mental phenomena, which are a part of its complete evolution, are very interesting in themselves. The disease is proved to be due to the use of Indian corn, associated with *penicillium glaucum*. The symptoms vary in different parts of Italy. Lombroso studied 472 cases in several places. He classes them under these varieties: the worst, and rarest, is a rapidly-progressing urinæmia, depending upon atrophy or degeneration of the kidneys; in another class of cases rapid and extraordinary emaciation occurs; in others irritation of the urinary, genital or digestive organs is the most prominent symptom.

Among the skin affections, patches of chloasma and maculæ seem to be the earliest; sometimes the whole surface of the body becomes darkened; erythema, herpes, and eczema are also ob-

served ; but all of these are not so common as most persons who merely read pellagra in books might suppose.

In many cases the nervous system is the chief sufferer. Sometimes without any other morbid symptoms, patients suffer from constant vertigo and considerable muscular weakness. Partial chorea, epileptiform convulsions, tremor and paraplegia are seen in apparently well-nourished patients. A feeling of heat in the hands and feet is common ; pruritus and formication or numbness are frequently complained of. Violent unilateral headache with dilatation of pupil on same side is very common. Deafness and ptosis are not uncommon. Retinal disease is observed in two-thirds of the cases. Great mental impressionability or irritability of temper is characteristic, occasionally ordinary melancholia, more rarely monomania occurs. A real or apparent stupidity, an obstinate mutism, is tolerably common. Many patients complain of hallucinations, evidently connected with their morbid visceral states. But as a rule their insanity is of a misty, ill-defined, contradictory character, like that produced by old age or by anæmia, and differing in this point from general peralalysis. Refusal of food is a particularly common symptom. A fondness for getting into or seeing water is characteristic and is called "*hydromania*." But the very opposite may occur—a profound dislike for the sight or touch of water, due to a vertigo that water produces. Suicide by drowning is very common.

We wish especially to express our obligations to Doctors J. J. Watson, D. S. Pope, and L. K. Philpot, of Columbia, and to Doctors Robert Wilson, Jr., chairman, and C. P. Williams, secretary of your board, for advice and assistance regarding our problem, as well as in determining upon the best method of laying the matter before the profession of our State. Dr. Ch. Wardell Stiles, of the U. S. Public Health and Marine-Hospital Service, also studied one of our cases and encouraged us in the work we were trying to do.

Our thanks are also due to Dr. G. T. Tuttle, superintendent McLean Hospital, Waverley, Mass., Dr. F. B. Mallory, of the Harvard Medical School, Boston ; Dr. W. H. Doughty, Jr., of Augusta, Ga., and to Drs. Walter D. McGaw and Robert Fletcher and Mr. H. C. Hall, of the Army Medical Museum and Library,

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Respectfully submitted,

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CASE I.





CASE III.



CASE II.

